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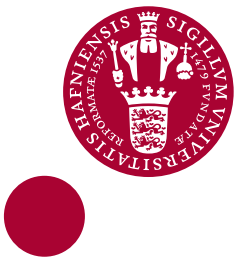

9-tetrahydrocannabinol

harmful even in low doses?

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to differences in change (ie, some items are more or less likely to detect differences between treatments).[5,6] Which items should be included in the scales used in future trials of various treatments for depression? Should they be dependent on the treatments (eg, drugs, psychotherapies, neuromodulations), populations (eg, adolescents, adults, elderly people), or subtypes of depression examined? Good studies generate more questions than they answer. And good datasets allow us to ask important questions in rigorous ways. I thank Bondar and colleagues and the original investigators of TADS for their work, and welcome the increasingly common trend of data sharing.[7]

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Δ^9-tetrahydrocannabinol: harmful even in low doses?


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Cannabis is a substance that is shrouded in myth, paradox, and controversy. On the one hand, a host of literature indicates detrimental effects on areas such as mental health (eg, increased risk of schizophrenia and poorer prognosis among patients with psychiatric disorders who also use cannabis), risk of addiction, and psychosocial functioning.[1–4] On the other hand, there has been an increase in public perception of cannabis as relatively harmless, as well as international movements to legalise cannabis for medicinal or recreational purposes.[5] Of course, this does not necessarily constitute a paradox—benzodiazepines and opioids are also used both recreationally and medicinally, and with both positive (eg, reduction of pain or anxiety) and negative (eg, addiction or death) effects.

However, the controversy appears to run deeper in the case of cannabis, probably because of the counterculture that has existed around the substance for the past 50 years. Cannabis is increasingly seen as harmless, perhaps because it is a natural product.[5] Observed negative effects on mental health are, in this viewpoint, seen as stemming solely from self-medication. This controversy has also existed in the scientific community. Within a rather short time period, two systematic reviews were published in *The Lancet*.[1,6] The first concluded that the associations between cannabis and psychosis were most likely explained by non-causal or selection mechanisms.[6] The second concluded that, although causality between cannabis and psychosis was difficult to establish, there was ample reason to be cautious because evidence was pointing in this direction.[1] Since then, much research has been published, and there appears to be a growing scientific consensus that cannabis does have a causal role in the development of psychosis. Indeed, the association appears to be bidirectional, so both hypotheses are probably correct.[7,8] In some people, cannabis leads to incident psychosis, whereas in other people, psychosis leads to incident cannabis use.

This growing scientific consensus is not reflected in the mainstream public discourses, which have a major effect on the political agenda to decriminalise or legalise cannabis. It also appears that, in many places (eg, several US states), the first thing to be legalised is medicinal cannabis followed by increasing decriminalisation and sometimes complete legalisation of cannabis. It is thus of utmost importance that the public and politicians are informed of the most up-to-date evidence on cannabis. Adding to the state of this evidence is the

systematic review and meta-analysis by Guy Hindley and colleagues[9] in *The Lancet Psychiatry*. The authors demonstrate that Δ⁹-tetrahydrocannabinol (THC) leads to an increase in total symptoms, which was assessed in nine studies, with ten independent samples, involving 196 participants: standardised mean change in scores (assessed with the Brief Psychiatric Rating Scale and the Positive or Negative Syndrome Scale) 1·10 (95% CI 0·92–1·28, p<0·0001). The effect sizes were also large for other symptoms (including general psychiatric symptoms), and were induced even with low doses of THC, somewhat similar to the doses often seen in medicinal cannabis, which we find extremely important and worrying. Moreover, the authors failed to find any clear evidence that concurrent administration of cannabidiol (CBD) reduced these symptoms. Indeed, such an ameliorating effect was observed in only one of four included studies. This finding is notable because CBD in particular is being touted as a potential wonder drug with antipsychotic, anxiolytic, and other properties.[10] Although it is quite possible that CBD will have some therapeutic applications (once proper randomised trials have been done), this supports suggestions that many of the initial reports and public discourses regarding the usefulness of both pure CBD and whole-plant-based extracts of cannabis might be somewhat exaggerated compared with what we can expect in clinical practice. Finally, although THC, alone or in combination with, for example, CBD might have a role in treating certain symptoms, caution should not be thrown to the wind. As Hindley and colleagues have clearly demonstrated, there are at least transient psychiatric symptoms associated with even relatively low doses of THC. Of course, this result should not be extrapolated as meaning that single doses of THC will eventually lead to schizophrenia or other severe disorders. However, it might be prudent to extrapolate and paraphrase the words of Moore and colleagues from their 2007 meta-analysis to apply to both recreational and medicinal use of THC-containing cannabis: "there is sufficient evidence to warn people that using THC could increase their risk of developing psychiatric symptoms or even a psychotic illness".[1]

We declare no competing interests.

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Digital phenotyping: hype or hope?

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In September, 2018, Thomas Insel speculated that, in 2050, psychiatrists will have realised that "the revolution in technology and information science will prove more consequential for global mental health," compared with the developments in genomics and neuroscience.[1] This is an astounding statement in itself, especially from somebody who advocated genomics and neuroscience[2] in his former position as head of The National Institute of Mental Health. However, what exactly is meant by information science and why should it outpace neuroscience and genetics?

Digital phenotyping refers to the moment-to-moment quantification of human behaviour in everyday life using data from personal digital devices.[3,4] This process will, according to Insel, overcome challenges in mental health by providing objective assessments of symptomatology